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THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

BEUG *et al.*

Appl. No. 10/086,073

Filing Date: March 1, 2002

For: **Pharmaceutical Compositions for
Treating Tumour Diseases**

Confirmation No: 3217

Art Unit: 1642

Examiner: *To be assigned*

Atty. Docket: 0652.1790001/EKS/BEC

Information Disclosure Statement

Assistant Commissioner for Patents
Washington, D.C. 20231

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Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of each of these documents is provided.

Document AP1 is in the German language with an English language abstract. The relevance of document AP1 can be ascertained by reference to page 26, lines 23-25, of the application as filed.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith. It is further understood that the Examiner will consider information that had been cited or submitted to the U.S. Patent and Trademark Office in a prior application relied on under 35 U.S.C. § 120. 1138 OG 37, 38 (May 19, 1992).

This Information Disclosure Statement is being submitted more than three months after the filing date, but before the first mailing of an Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and to indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

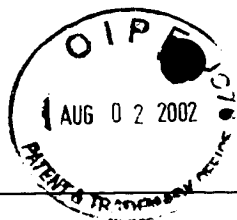
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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Attorney for Applicants
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Date: August 2, 2002

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U.S. PATENT DOCUMENTS

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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB- CLASS	TRANSLATION
	AL1	WO 91/19513 A1	12/26/1991	WIPO			Yes No
	AM1	EP 0 604 181 A1	06/29/1994	Europe			Yes No
	AN1	WO 94/25588 A2	11/10/1994	WIPO			Yes No
	AO1	WO 95/19987 A1	07/27/1995	WIPO			Yes No
	AP1	WO 96/07657 A1	03/14/1996	WIPO			Yes No

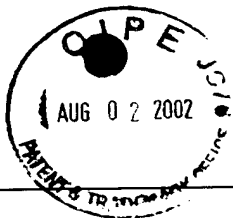
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>1</u>	Andrejauskas, E., and Moroni, C., "Reversible abrogation of IL-3 dependence by an inducible H-ras oncogene," <i>EMBO J.</i> 8:2575-2581, IRL Press (1989)
	AS	<u>1</u>	Antonelli-Orlidge, A., et al., "An activated form of transforming growth factor β is produced by cocultures of endothelial cells and pericytes," <i>Proc. Natl. Acad. Sci. USA</i> 86:4544-4548, National Academy Press (1989)
	AT	<u>1</u>	Beham, A., et al., "Distribution of cytokeratins, vimentin and desmoplakins in normal renal tissue, renal cell carcinomas and oncocytoma as revealed by immunofluorescence microscopy," <i>Virchows Archiv. A Pathol. Anat.</i> 421:209-215, Springer-Verlag (1992)

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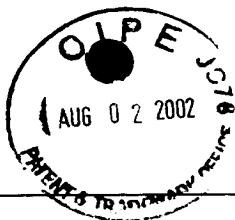
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	2	Braunwalder, A.F., et al., "Measurement of the Protein Tyrosine Kinase Activity of c-src Using Time-Resolved Fluorometry of Europium Chelates," <i>Anal. Biochem.</i> 238:159-164, Academic Press, Inc. (July 1996)
AS	2	Buchmann, A., et al., "Progression of Squamous Carcinoma Cells to Spindle Carcinomas of Mouse Skin Is Associated with an Imbalance of H-ras Alleles on Chromosome 7," <i>Cancer Res.</i> 51:4097-4101, American Association for Cancer Research (1991)
AT	2	Castle, V., et al., "Antisense-mediated Reduction in Thrombospondin Reverses the Malignant Phenotype of a Human Squamous Carcinoma," <i>J. Clin. Invest.</i> 87:1883-1888, American Society for Clinical Investigation (1991)

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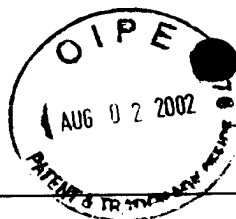
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	3	Caulin, C., et al., "Chronic Exposure of Cultured Transformed Mouse Epidermal Cells to Transforming Growth Factor- β , Induces an Epithelial-Mesenchymal Transdifferentiation and a Spindle Tumoral Phenotype," <i>Cell Growth Differ.</i> 6:1027-1035, American Association for Cancer Research (August 1995)
	AS	3	DeBortoli, M.E., et al., "Amplified Expression of p21 ras Protein in Hormone-Dependent Mammary Carcinomas of Humans and Rodents," <i>Biochem. Biophys. Res. Commun.</i> 127:699-706, Academic Press, Inc. (1985)
	AT	3	de Brito, P.A., et al., "Carcinosarcoma (Malignant Mixed Müllerian (Mesodermal) Tumor) of the Female Genital Tract: Immunohistochemical and Ultrastructural Analysis of 28 Cases," <i>Hum. Pathol.</i> 24:132-142, W.B. Saunders Company (1993)

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	4	Eaton, S., and Simons, M., "Apical, Basal, and Lateral Cues for Epithelial Polarization," <i>Cell</i> 82:5-8, Cell Press (July 1995)
	AS	4	Fakhrai, H., et al., "Eradication of established intracranial rat gliomas by transforming growth factor β antisense gene therapy," <i>Proc. Natl. Acad. Sci. USA</i> 93:2909-2914, National Academy Press (April 1996)
	AT	4	Furth, M.E., et al., "Monoclonal Antibodies to the p21 Products of the Transforming Gene of Harvey Murine Sarcoma Virus and of the Cellular ras Gene Family," <i>J. Virol.</i> 43:294-304, American Society for Microbiology (1982)

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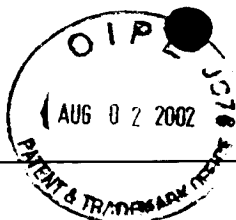
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>5</u>	Guarino, M., et al., "Carcinosarcoma of the oesophagus with rhabdomyoblastic differentiation," <i>Histopathology</i> 22:493-498, Blackwell Scientific Publications (1993)
	AS	<u>5</u>	Hand, P.H., et al., "Monoclonal antibodies of predefined specificity detect activated <i>ras</i> gene expression in human mammary and colon carcinomas," <i>Proc. Natl. Acad. Sci. USA</i> 81:5227-5231, National Academy Press (1984)
	AT	<u>5</u>	Hay, E.D., "An Overview of Epithelio-Mesenchymal Transformation," <i>Acta Anat.</i> 154:8-20, S. Karger Medical and Scientific Publishers (March 1996)

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	6	Heatley, M., et al., "Vimentin expression in benign and malignant breast epithelium," <i>J. Clin. Pathol.</i> 46:441-445, BMJ Publishing Group (1993)
	AS	6	Hoosein, N.M., et al., "Differential Sensitivity of Subclasses of Human Colon Carcinoma Cell Lines to the Growth Inhibitory Effects of Transforming Growth Factor- β 1," <i>Exp. Cell Res.</i> 181:442-453, Academic Press, Inc. (1989)
	AT	6	Jenkins, D.C., et al., "A novel cell-based assay for the evaluation of anti-ras compounds," <i>Br. J. Cancer</i> 68:856-861, Macmillan Press, Ltd. (1993)

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FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>	ATTY. DOCKET NO. 0552.1790001/EKS/BEC	APPLICATION NO. 10/086,073
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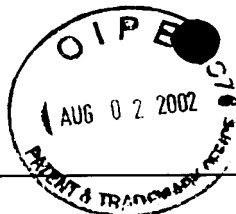
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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	7	Kern, F.G., et al., "Growth factor receptors and the progression of breast cancer," <i>Semin. Cancer Biol.</i> 1:317-328, W.B. Saunders Company (1990)
	AS	7	Keski-Oja, J., et al., "Transforming Growth Factors and Control of Neoplastic Cell Growth," <i>J. Cell. Biochem.</i> 33:95-107, Alan R. Liss, Inc. (1987)
	AT	7	Kim, S.-J., et al., "Promoter Sequences of the Human Transforming Growth Factor- β 1 Gene Responsive to Transforming Growth Factor- β 1 Autoinduction," <i>J. Biol. Chem.</i> 264:7041-7045, American Society for Biochemistry and Molecular Biology, Inc. (1989)

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>8</u>	Kohl, N.E., et al., "Selective Inhibition of ras-Dependent Transformation by a Farnesyltransferase Inhibitor," <i>Science</i> 260:1934-1937, American Association for the Advancement of Science (1993)
	AS	<u>8</u>	Kohl, N.E., et al., "Protein farnesyltransferase inhibitors block the growth of ras-dependent tumors in nude mice," <i>Proc. Natl. Acad. Sci. USA</i> 91:9141-9145, National Academy Press (1994)
	AT	<u>8</u>	Kohl, N.E., et al., "Inhibition of farnesyltransferase induces regression of mammary and salivary carcinomas in ras transgenic mice," <i>Nat. Med.</i> 1:792-797, Nature Publishing Company (August 1995)

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
AR	<u>2</u>	LeJeune S., et al., "Amphiregulin, Epidermal Growth Factor Receptor, and Estrogen Receptor Expression in Human Primary Breast Cancer," <i>Cancer Res.</i> 53:3597-3602, American Association for Cancer Research (1993)	
AS	<u>2</u>	Lin, H.Y., et al., "Expression Cloning of the TGF- β Type II Receptor, a Functional Transmembrane Serine/Threonine Kinase," <i>Cell</i> 68:775-785, Cell Press (1992); erratum, <i>Cell</i> 70:1068, Cell Press (1992)	
AT	<u>2</u>	Matsui, K., et al., "Lung Carcinoma With Spindle Cell Components: Sixteen Cases Examined by Immunohistochemistry," <i>Hum. Pathol.</i> 23:1289-1297, W.B. Saunders Company (1992)	

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>10</u>	Miettinen, P.J., et al., "TGF- β Induced Transdifferentiation of Mammary Epithelial Cells to Mesenchymal Cells: Involvement of Type I Receptors," <i>J. Cell Biol.</i> 127:2021-2036, Rockefeller University Press (1994)
	AS	<u>10</u>	Monia, B.P., et al., "Sequence-specific antitumor activity of a phosphorothioate oligodeoxyribonucleotide targeted to human C-raf kinase supports an antisense mechanism of action in vivo," <i>Proc. Natl. Acad. Sci. USA</i> 93:15481-15484, National Academy Press (December 1996)
	AT	<u>10</u>	Murthy, U., et al., "Expression of TGF- α /EGF and TGF- β Receptors in Human Colon Carcinoma Cell Lines," <i>Int. J. Cancer</i> 44:110-115, Alan E. Liss, Inc. (1989)

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	AR	11	Nishihara, K., and Tsuneyoshi, M., "Undifferentiated Spindle Cell Carcinoma of the Gallbladder: A Clinicopathologic, Immunohistochemical, and Flow Cytometric Study of 11 Cases," <i>Hum. Pathol.</i> 24:1298-1305, W.B. Saunders Company (1993)
	AS	11	Oft, M., et al., "TGF- β 1 and Ha-Ras collaborate in modulating the phenotypic plasticity and invasiveness of epithelial tumor cells," <i>Genes Dev.</i> 10:2462-2477, Cold Spring Harbor Laboratory Press (October 1996)
	AT	11	Parker, T.G., et al., "Peptide Growth Factors Can Provoke 'Fetal' Contractile Protein Gene Expression in Rat Cardiac Myocytes," <i>J. Clin. Invest.</i> 85:507-514, American Society for Clinical Investigation, Inc. (1990)

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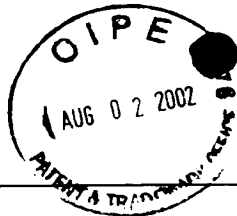
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	AR	<u>12</u>	Payne, P.A., et al., "An activated c-Ha-ras allele blocks the induction of muscle-specific genes whose expression is contingent on mitogen withdrawal," <i>Proc. Natl. Acad. Sci. USA</i> 84:8956-8960, National Academy Press (1987)
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ATTY. DOCKET NO.
0652.1790001/EKS/BECAPPLICATION NO.
10/086,073APPLICANTS
Beug et al.FILING DATE
March 1, 2002GROUP
1642

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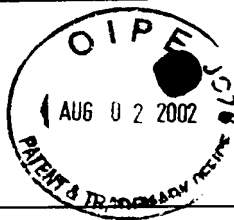
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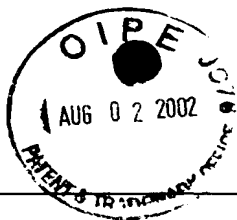
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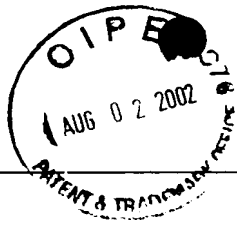
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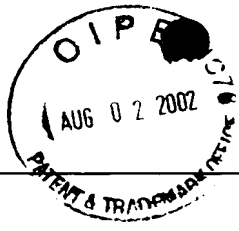
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August 2, 2002

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Art Unit 1642

Re: U.S. Utility Patent Application
Appl. No. 10/086,073; filed March 1, 2002
For: **Pharmaceutical Compositions for Treating Tumour Diseases**
Inventors: Beug *et al.*
Our Ref: 0652.1790001/EKS/BEC

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Information Disclosure Statement;
2. Form PTO-1449 (19 sheets) and accompanying (62) references; and
3. Return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Commissioner for Patents

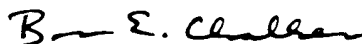
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The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Bruce E. Chalker
Attorney for Applicants
Registration No. 47,480

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Enclosures